

In re: Bentley  
Appl. No.: 09/678,997  
Filed: October 4, 2000  
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#### REMARKS

Applicant confirms its election of the claims of Group I, which are Claims 1 through 16. Claims 1 through 16 have been cancelled and new Claims 30 through 50 have been submitted. Claims 17 through 29 have been cancelled as non-elected. The redrafted claims do not contain the phrases rejected on the basis of indefiniteness and so these rejections should be obviated. All of Claims 1 through 16 were rejected as unpatentable over Patel et al. (Bioconjugate Chem., vol. 8, p. 434 through 441, 1997). However, prior to considering the Patel article, it should be useful to consider Applicants' invention as recited in the pending claims.

The invention provides novel and nonobvious substantially hydrophilic conjugates of water soluble, nonpeptidic polymers with particular peptides, including the synthetic peptides biphalin and [D-Pen<sup>2</sup>, D-Pen<sup>5</sup>] enkephalin (DPDPE). Synthetic peptides conjugated to nonpeptidic polymers at various molecular weights, are exemplified to have the property of entering the brain from the general circulation instead of being trapped in capillaries and to exhibit potent analgesic effect. The term "substantially hydrophilic" is defined in the specification at page 5, lines 20 through 24, to mean that the conjugate does not contain a substantially lipophilic moiety such as fatty acids or glycolipids. Fatty acids and glycolipids are used in the art to increase the lipophilicity of a molecule to increase the ability of the molecule to pass cell membranes. By contrast, the ability of the conjugates of the invention to cross the blood brain barrier and to retain and exhibit potent analgesic effect is unexpected.

The invention also includes conjugates as described that further comprise neuroactive substances generally.

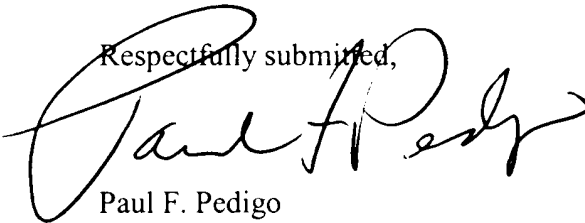
In sharp contrast to the invention, the Patel et al. article describes the heptapeptide deltorphin conjugated to a "highly lipophilic" triglyceride that has lipophilic tethers attached. None of the conjugates of the invention, based on water-soluble, nonpeptidic polymers, in the absence of substantially lipophilic moieties, is disclosed or suggested.

The newly submitted claims clearly define conjugates and pharmaceutical compositions that are neither disclosed or suggested by any of the references of record, considered alone or in

combination. Accordingly, reconsideration by the Examiner and an early indication of the allowability of the pending claims are earnestly solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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Elaine Kelly